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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	17

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/914,332	Applicant(s) Van Arsdell et al.
	Examiner Peter Tung	Group Art Unit 1652

X Responsive to communication(s) filed on *Jun 4, 1999* .

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *1-31* is/are pending in the application.

Of the above, claim(s) *23-31* is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) *1, 2, and 6-22* is/are rejected.

X Claim(s) *3-5* is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____ .

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

X Information Disclosure Statement(s), PTO-1449, Paper No(s). *14,15*

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 11 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is explained in the previous Office action.

3. Applicants argue that guidance on obtaining a bacterium which is deregulated in one biotin synthetic pathway step other than *bioA* is provided in the specification, which teaches various ways to deregulate the KAPPA-to-DAPPA biosynthetic step. Four specific instances of the deregulation of lysine production from aspartate is provided as well as lysine deregulated mutants.

Response to Arguments

4. Applicant's arguments filed 6/4/99 have been fully considered but they are not persuasive. The specification does not provide sufficient teaching on deregulating the KAPPA-to DAPPA biosynthetic step. Specific strains are provided with a description of the DNA cassettes used to make those strains which are deregulating in the KAPPA-to-DAPPA biosynthetic pathway.

Without the DNA sequences of the specific cassettes i.e. P_{15}*bio* or the deposit of those strains, one of ordinary skill in the art would not be able to make and use a bacterium with a deregulated KAPPA-to DAPPA biosynthetic pathway. Additionally, it is not clear where the *bio* locus is disrupted by the DNA cassettes as the *bio* locus also includes *bioA*.

While four specific instances of the deregulation of lysine production from aspartate are provided as well as lysine deregulated mutants, the instant claim is drawn to a bacterium with a deregulated biotin biosynthetic pathway. The examples provided by the Applicant are for a lysing biosynthetic pathway.

5. Claims 9, 10 and 13-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The bacterium resistant to S-2-aminoethyl-L-cysteine and the bacterium engineered to produce a SAM-utilizing DAPA aminotransferase must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. *See 37 CFR 1.808.* Further, the record must be clear

that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample **or for the enforceable life of the patent whichever is longer.** See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met. Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 6, 7 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Levy-Schil et al. Levy-Schil et al. teach (page 755, "Bacterial strains and media," "Biotin and vitamer quantification") a method of making biotin by culturing E. coli in a medium comprising casamino acids and purifying the biotin produced. Casamino acids comprise lysine and aspartate, a lysine precursor. The instant claims are therefore anticipated by Levy-Schil et al.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy-Schil et al. in view of Yamada et al. (U.S. Patent No. 4,563,426). The teachings of Levy-Schil et al. have been discussed supra. Claim 8 adds the further limitation of converting the recovered dethiobiotin to biotin by a separate process. Levy-Schil et al. further teach (page 755, "Bacterial strains and media," "Biotin and vitamer quantification") a method of making dethiobiotin by culturing *E. coli* in a medium comprising casamino acids and purifying the dethiobiotin produced.

Levy-Schil et al. do not teach converting dethiobiotin to biotin by a separate process. Yamada et al.(U.S. Patent No. 4,563,426) teach (column 1, lines 40-66) a method of producing biotin by adding dethiobiotin to a fermentation medium. Yamada et al. do not teach dethiobiotin production. It would have been obvious to one of ordinary skill in the art at the time the invention was made to convert the dethiobiotin produced as taught by Levy-Schil et al., into biotin as taught by Yamada et al., for the benefit of producing biotin. One of ordinary skill in the art is motivated to combine the teachings as Levy-Schil et al. show a method of making dethiobiotin and the teachings of Yamada et al. show how to produce biotin from dethiobiotin. One of ordinary skill in the art would have a reasonable expectation of success at doing this as the teachings of Levy-Schil et al. show a method of making dethiobiotin, which is a starting material for making biotin, as shown by the teachings of Yamada et al. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

10. Claims 1, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy-Schil et al. in view of Komatsubara et al. (U.S. Pat. No. 5,374,554). The teachings of Levy-Schil et al. have been discussed supra. Claims 9 and 10 add the further limitation of a bacterium resistant to the lysine analog S-2-aminoethyl-L-cysteine. Levy-Schil et al. do not teach a bacterium resistant to the lysine analog S-2-aminoethyl-L-cysteine. Komatsubara et al. (U.S. Pat. No. 5,374,554) teach a *Searratia* strain resistant to S-2-aminoethyl-L-cysteine which is used for biotin production. Komatsubara et al. do not teach using lysine or a lysine precursor in the growth media for said *Serratia* strain for the production of biotin. It would have been obvious to

one of ordinary skill in the art at the time the invention was made to produce biotin using the Serratia strain resistant to S-2-aminoethyl-L-cysteine, as taught by Komatsubara et al. using the growth media taught by Levy-Schil et al. for the benefit of growing the Serratia in a rich medium. One of ordinary skill in the art is motivated to do this as a rich medium would provide extra nutrients and allow the faster growth of the bacteria. One of ordinary skill in the art has a reasonable expectation of success at doing this as bacteria are grown in many different media and the use of a rich medium (casamino acids are provided) to improve the growth of bacteria is well known in the art. As casamino acids comprise lysine and aspartate, a lysine precursor, the limitations of claim 1 are anticipated. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

11. Claims 3, 4, 5 and 13-22 are allowable over the prior art of record. The prior art of record does not teach or suggest a method of making biotin using an overproducer of lysine-utilizing DAPA aminotransferase or also expressing additional SAM-utilizing DAPA aminotransferase.

12. Claims 3, 4 and 5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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